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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/537,149	12/22/2005	Ying Wu	65959/51	1703

1912 7590 06/01/2007

AMSTER, ROTHSTEIN & EBENSTEIN LLP
90 PARK AVENUE
NEW YORK, NY 10016

EXAMINER	
GREENE, JAIME M	
ART UNIT	PAPER NUMBER
1609	
MAIL DATE	DELIVERY MODE
06/01/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/537,149	WU ET AL.	
	Examiner	Art Unit	
	Jaime M. Greene	1609	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *26 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *36-62* is/are pending in the application.

4a) Of the above claim(s) *51-62* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *36-50* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *02 June 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election of group 1 and election of species poly-l-lysine in the reply filed on 3/22/07 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claims 51-62 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 3/22/07.

Information Disclosure Statement

3. The information disclosure statement filed 6/3/05 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein that does not contain a corresponding copy has not been considered, said not considered reference being indicated by a line drawn through the reference in the IDS.

Claim Objections

4. Claim 36 is objected to because of the following informalities: the claim preamble recites "a method for hybridization of probes onto immobilized genomic DNA"

(lines 1-2), whereas the method steps refer only to genomic content (lines 4, 6, 7,12 and 14), which creates a lack of consistency within the claim. Appropriate correction is required.

Claim Rejections - 35 USC § 112

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claim 36-50 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7. Claim 36 recites the limitation "leaving formed hybridized intact genomic content/probe complexes for further analysis" (lines 13-14). However, it is unclear what genomic content/probe means, as the slash "/" can have several meanings, including being used in place of the word "or". Claims 37-50 depend from claim 36 and do not solve the problem. Applicant is required to clarify.

8. Claim 46 refers to flow rates in the units mm/min, however, flow rate is defined as "the amount of fluid that flows in a given time" (http://www.thefreedictionary.com/), and since fluids are measured in volume and not distance, it is unclear what applicant means by a flow rate measured in mm/min. Applicant is required to clarify.

9. Claim 46 also recites the limitation "comprised between", suggesting a limited range, however the term comprising (and thereby comprised) "is inclusive or open-ended and does not exclude additional, unrecited elements" (See MPEP 2111.03).

Therefore, it is unclear what applicant regards as a flow rate "comprised between". Applicant is required to clarify.

Claim Rejections - 35 USC § 103

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

11. Claims 36, 37, 39, 40-44, 46, 47 and 50 rejected under 35 U.S.C. 103(a) as being unpatentable over Armour (Armour, et al. Measurement of locus copy number by hybridisation with amplifiable probes. Nucleic Acids Res. 2000 Jan 15;28(2):605-9.) in view of by Tam (Tam, US Patent Number 5741647).

Regarding claims 36, 37, 40, 41, 42, 43, and 50 Amour teaches "In this report we show that short amplifiable probes can be recovered quantitatively after hybridization to genomic DNA" (page 605, column 2, paragraph 1) (i.e. claim 36, a method for hybridization of probes onto immobilized genomic DNA). Amour teaches "Genomic DNA for immobilisation (0.5–1 μg) was prepared in an initial volume of <5 μl, denatured by addition of 1 μl 1 M NaOH, spotted onto an individual nylon filter (MSI MAGNA, dimensions ~2 x 4 mm), and irreversibly bound to the filter by UV irradiation" (page 605, column 2, paragraph 3) (i.e. claim 36, providing a sample containing or suspected of having genomic content, wherein said genomic content is undigested or intact chromosomal DNA or RNA) (i.e. claim 36, denaturing said intact genomic content) (i.e.

claim 36, immobilizing said denatured intact genomic content within a matrix) (i.e. claim 37, wherein said denatured intact genomic DNA is permeated within said matrix) (i.e. claim 40, wherein said matrix is a membrane) (i.e. claim 41, wherein said membrane comprises a 3D network structure) (i.e. claim 42, wherein said network structure is a flow-through structure) (i.e. claim 43, wherein said network structure is a fibre network structure). Armour teaches that "probes were prepared" (page 605, column 2, paragraph 2); that "the probe mixture was placed on ice, neutralised by adding 3 µl 1 M NaH_2PO_4, and added to the hybridisation solution" (page 606, column 1, lines 1-2); and that "hybridisation was left to proceed at 65°C overnight" (page 606, column 1, paragraph 1) (i.e. claim 36, providing a set of probes and passing said probes through the said matrix under conditions favoring hybridization of the probes to its complementary sequence in said intact genomic content). Armour teaches that "the filters were washed" (page 606, column 1, paragraph 1) (i.e. claim 36, washing off non-hybridized probe through said matrix, leaving formed hybridized intact genomic content/probe complexes for further analysis). Armour also teaches that "probes were prepared by...probe DNA amplified directly from bacterial cells using flanking vector primers (page 605, column 2, paragraph 2) (i.e. claim 50, wherein said probes are flanked by primer binding sequences).

Regarding claim 36, Armour does not teach that the matrix comprises pore sizes within a range of 0.6µm to 2µm including the outer limits. However, Tam teaches "flow through nucleic acid hybridization (title) and that "the membrane can be any type such as the nitrocellulose, nylon, Nytran, or the Biodynes as long as it is capable of

immobilizing DNA sequences (column 6, lines 21-24). One of ordinary skill in the art would be motivated to use a matrix with pore sizes in the within a range of 0.6μm to 2μm, because membranes with such pore sizes are commonly used in the art for immobilizing DNA to a membrane. There is a reasonable expectation that immobilizing genomic DNA, per the method of Armour, to a membrane with pore sizes in the within a range of 0.6μm to 2μm would be successful because it is suggested in the method of Tam and is commonly performed in the art. Therefore, it would have been prima facie obvious at the time the invention was made to immobilize genomic DNA onto a membrane with pore sizes within a range of 0.6μm to 2μm because it is commonly performed in the art, absent evidence to the contrary.

Regarding claim 39, Armour does not teach "wherein said washing step is carried out by passing through said matrix a wash fluid by at least one cycle of downwards flow. However, Tam teaches a protocol used in the flow-through process (column 10, lines 27-28) that includes washing (column 10, lines 43-44 and 47-48) and that the liquids flow downward (column 9, lines 23-24). One of ordinary skill in the art would be motivated to wash the membrane of Armour with at least one cycle of downwards flow in order to speed up the washing process. There is a reasonable expectation that washing the membrane of Armour with at least one cycle of downwards flow would be successful because it is successfully accomplished by the method of Tam. Therefore, it would have been prima facie obvious at the time the invention was made to, absent evidence to the contrary.

Regarding claims 44, Armour does not teach that said fibre is of vegetable origin. However Tam teaches that "the membrane can be any type such as the nitrocellulose, nylon, Nytran, or the Biodynes as long as it is capable of immobilizing DNA sequences (column 6, lines 21-24). One of ordinary skill in the art would be motivated to use a nitrocellulose membrane (i.e. of vegetable origin) for the method of Armour, because it is commonly used in the art as a membrane for immobilizing DNA. There is a reasonable expectation that nitrocellulose membrane would be successfully used in the method of Armour, because, as described by Tam, nitrocellulose, like nylon, can also be used to immobilize DNA. Therefore, it would have been prima facie obvious at the time the invention was made to use a nitrocellulose membrane with the method of Armour because it is one of the commonly used membranes for immobilizing DNA, absent evidence to the contrary.

Regarding claim 46, Armour does not teach "wherein the matrix allows for a flow rate comprised between 50mm/30min and 250mm/30min including the outer limits. However, Tam teaches that "the control of flow rate as well as the direction can be regulated" (column 6, lines 31-32). Also, it should be noted that ""[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." In re Aller, 220 F.2d 454, 456, 105 USPQ 233, 235 (CCPA 1955)" (See, MPEP 2144.05). One of ordinary skill in the art would be motivated to use a range of flow rates in order to optimize the conditions for hybridization. There is a reasonable expectation that a range of flow rates could be used successfully with the method of Armour, because Tam teaches the use of the

matrix of Armour and Tam teaches testing a variety of flow rates with a membrane. Therefore, it would have been prima facie obvious to use a range of flow rates with the membrane of Armour in order to optimize the conditions for hybridization, absent evidence to the contrary.

Regarding claim 47, Armour does not teach that said matrix is activated with an affinity conjugate. However, Tam teaches that the membrane can first be coated with an affinity conjugate such as avidin to form the activated membrane (column 6, lines 15-17). One of ordinary skill in the art would be motivated to activate the membrane with an affinity conjugate as an alternative means of binding the DNA to the membrane. There is a reasonable expectation that activating the membrane of Armour with an affinity conjugate would be successful because affinity conjugates are commonly used in the art on membranes as a means of immobilizing DNA. Therefore, it would have been prima facie obvious at the time the invention was made to add an affinity conjugate to the membrane of Armour as a common means of immobilizing the genomic DNA to the membrane, absent evidence to the contrary.

12. Claim 38 rejected under 35 U.S.C. 103(a) as being unpatentable over Armour and Tam, as applied to claim 36 above, further in view of Sommers (Sommers, et al, US Patent Application Publication Number 20040101444). As described above, Armour and Tam teaches all the limitations of claim 36, from which claim 38 depends. However, while Tam teaches that "the control of flow rate as well as the direction can be regulated by the difference in design of the gasket" (column 6, lines 31-35), Armour and Tam do

not specifically teach that the probes are passed through the matrix by upward and downward flow.

Sommers teaches "A fluid circuit [that] may be used to transfer a test reagent or sample to a...[DNA chip] and that "the fluid flow may be reversed across the chip by the use of a reversible pump" (page 3, paragraph 52) (i.e. probes are passed through said matrix by at least one cycling of upward and downward flow). One of ordinary skill in the art would be motivated to reverse the flow of probe as described by Sommers over the membrane of Armour and Tam for "improving hybridization...efficiencies" (Sommers, page 12, paragraph 143). There is a reasonable expectation that the reversal of fluid flow of Sommers as part of the hybridization method of Armour and Tam would be success because methods applied to nucleic acid hybridization techniques are used transferably in the art, and Tam suggests said modification ("the control of flow rate as well as the direction can be regulated by the difference in design of the gasket"; column 6, lines 31-35). Therefore it would have been prima facie obvious at the time the invention was made to improve the method of Armour and Tam by reversing the flow of nucleic acids over the matrix as a means of improving hybridization efficiency, absent evidence to the contrary.

13. Claims 45, 48, and 49 rejected under 35 U.S.C. 103(a) as being unpatentable over Armour and Tam as applied to claims 44 and 47 above, further in view of Fish (Fish, et al. US Patent Number 5126276).

As described above, Amour teaches "Genomic DNA for immobilisation (0.5–1 μg) was prepared in an initial volume of <5 μl, denatured by addition of 1 μl 1 M NaOH,

spotted onto an individual nylon filter (MSI MAGNA, dimensions ~2 x 4 mm), and irreversibly bound to the filter by UV irradiation" (page 605, column 2, paragraph 3) and Tam teaches that "heat denatured...DNA of specific sequence... of various concentrations were immobilized onto the Nitrocellulose membrane" (column 10, lines 2-5). Tam also teaches that the membrane can first be coated with an affinity conjugate such as avidin to form the activated membrane (column 6, lines 15-17). However, Armour and Tam do not teach that the membrane is cellulose (claim 45) or that the affinity conjugate is poly-L-lysine (claims 48 and 49).

Fish teaches a "support...[that can be comprised of] various plastics e.g., polystyrenes and polyvinyls, as well as other polymeric materials, e.g., celluloses and nylons, as well as to glass fibers. (column 6, lines 63-67) (i.e. claim 45, said fiber is cellulose). Fish also teaches that "Double stranded nucleic acids do not bind to any significant extent to such surfaces such that when working with such materials two possible approaches are available, [and that] according to a first approach, the double stranded nucleic acid is bound by means of a cationic polymer such as poly-L-lysine to the support (column 7, lines 9-15) (i.e. claims 48 and 49, wherein said affinity conjugate is poly-L-lysine).

Regarding claim 45, One of ordinary skill in the art would motivated to use cellulose as the matrix because it's a commonly used membrane support for DNA in the art. Because cellulose is commonly used in the art as the matrix and affinity conjugate on the matrix for immobilizing DNA, and because Fish teaches that DNA can be immobilized on a support of cellulose, there is a reasonable expectation that a cellulose

matrix would be successfully used in the method of Armour and Tam for immobilizing DNA. Therefore, it would have been prima facie obvious at the time the invention was made to use the commonly known matrix cellulose as the membrane in the method of Armour and Tam, absent evidence to the contrary.

14. Regarding claims 48 and 49, one of ordinary skill in the art would be motivated to use poly-L-lysine because it's a commonly used affinity conjugate to bind DNA to a surface. Also because poly-L-lysine is commonly used in the art as the affinity conjugate on a matrix for immobilizing DNA, and because Fish teaches that DNA can be bound to a cellulose membrane by means of a cationic polymer such as poly-L-lysine, there is a reasonable expectation that a matrix with poly-L-lysine would be successfully used in the method of Armour and Tam for binding DNA. Therefore, it would have been prima facie obvious at the time to the invention was made to use the affinity conjugate poly-L-lysine on the membrane in the invention of Armour and Tam, absent evidence to the contrary.

Conclusion

No claims are allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jaime M. Greene whose telephone number is 571-270-3052. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, ALT. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mary Mosher can be reached on 571-272-0906. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

JMG 5/22/07

Jaime M. Greene

Sarae Bausch
Patent Examiner AU 1634